REMARKS

Claims 1 and 3-32 are pending in the application. Claims 14-32 have been withdrawn from consideration as being subject to nonelected inventions.

Claims 1 and 3-13 are subject to examination.

Response to Specification Objection

The specification has been corrected at pages 6 and 8, as suggested by Examiner. A typographical error on page 29 has also been corrected.

With respect to the Examiner's comments in paragraph 6 of the office action, referring to the text of the specification at page 9, lines 25-27, blue fluorescent protein, yellow fluorescent protein and cyan florescent protein are variants of green fluorescent protein. This is evidenced by page 4, lines 8 to 11 of the specification, and would be known to a person skilled in the art. In order to address the Examiner's clarity objection, the referenced passage from the specification has been amended to read: "Examples of fluorescent proteins include red fluorescent protein and variants of green fluorescent protein, such as blue fluorescent protein, yellow fluorescent protein and cyan fluorescent protein".

Response to 35 USC 112, 2nd Paragraph Rejection

Claim 1 has been rejected as allegedly indefinite. The Examiner alleges that it is unclear what modifications are included in "functionally associated with each other". In response, it is submitted that the expression "functionally associated with each other" in claim 1 refers to an association between complimentary fluorogenic fragments that results in the generation of a fluorescent signal. This functional association between complementary fluorogenic fragments occurs when a first peptide of interest in a bait fusion protein comprising the first fluorogenic fragment interacts with a second peptide of interest in a prey fusion protein comprising the complementary fluorogenic fragment.

The Examiner has commented that "it is unclear if the two fragments are functionally associated with each other, a fluorescent signal is generated, how a linker is interposed between the first and the second fluorogenic fragment, this would generate a fluorescent signal". In

response to the Examiner's comment, a linker is not interposed between the first and second fluorogenic fragments. Rather, a first linker portion is interposed between the first peptide and the first fluorogenic fragment of the bait fusion protein, and a second linker portion is interposed between a complementary fluorogenic fragment and a second peptide of interest of the prey fusion protein. Interaction of the first peptide with the second peptide (both peptides being linked to fluorogenic fragments) allows the fluorogenic fragments linked to these peptides to functionally associate with each other leading to the generation of a fluorescent signal. The mechanism by which complementary fragments of a fluorescent protein can generate a fluorescent signal when fused to proteins that interact with each other is referred to at page 4, lines 22 to 28 of the specification and is further described in the cited prior art document of Hu et al. wherein this process is referred to as "bimolecular fluorescence complementation (BiFC)".

Applicants therefore respectfully submit that claim 1, and dependent claims 3 to 13, clearly point out and distinctly claim the subject matter which they regard as their invention. A figure illustrating a prey and bait fusion protein of the protein interaction system is provided for the Examiner's reference as Appendix A.

Response to 35 USC 112 1st Paragraph Rejection – Written Description

Claims 1, 3 and 5-13 have been rejected under 35 U.S.C. 112, 1st paragraph, as allegedly failing to comply with the written description requirement. Reconsideration is requested in view of the following remarks.

A. The legal standard for determining compliance with the written description requirement.

To satisfy the written description requirement, the applicant must convey to the skilled artisan that, as of the filing date sought, the applicant was in possession of the invention. *See Falkner v. Inglis*, 448 F.3d 1357, 1365, 79 U.S.P.Q.2d 1001, 1007 (Fed. Cir. 2006). A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. *See, e.g., In re*

Marzocchi, 439 F.2d 220, 224, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971); *see also* MPEP § 2163.04.

The description needed to satisfy the requirements of 35 U.S.C. § 112 varies with the nature and scope of the invention at issue and with the scientific and technologic knowledge already in existence. *See, e.g., In re Wertheim,* 541 F.2d at 262, 191 U.S.P.Q. at 96 ("The primary consideration is *factual* and depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure") (emphasis in original); MPEP 2163 II.A.3.(a)(i); *Capon v. Eshhar*, 418 F.3d 1349, 1358, 76 U.S.P.Q.2d 1078, 1085 (Fed. Cir. 2005) ("The 'written description' requirement must be applied in the context of the particular invention and the state of the knowledge.").

This means that the description requirement is more easily met if a recited genus consists of compounds known in the art, e.g., fluorescent proteins, as opposed to a recited genus of hypothetical compounds. *Compare Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 926-27, 69 U.S.P.Q.2d, 1886, 1894-95 (Fed. Cir. 2004) (finding inadequate written description, where the disclosure provided nothing more than a "hoped-for function for ***an as-yet-to-be-discovered*** compound, and a research plan for trying to find it"), *with Capon*, 418 F.3d at 1358, 76 U.S.P.Q.2d at 1084-85 (reversing the Board and holding that functionally claimed chimeric genes prepared from ***known DNA sequences of known function*** were adequately described without a description of structure, formula, or chemical name for the nucleotide sequences).

That is, where a genus of compounds is already known in the art, the genus may be adequately described without providing detailed structures of a representative number of compounds within the genus. *See, e.g., In re Robins*, 429 F.2d 452, 456, 166 U.S.P.Q. 552, 555 (C.C.P.A. 1970) ("Mention of representative compounds encompassed by generic claim language clearly is not required by § 112 or any other provision of the statute."); *In re Herschler*, 591 F.2d 693, 700-01, 200 U.S.P.Q. 711, 717 (C.C.P.A. 1979) ("The solicitor urges that the class of steroids is so large that a single example in the specification could not describe the varied members with their further varied properties. We disagree with this contention."); *Falkner v. Inglis*, 448 F.3d 1357, 1365-66, 79 U.S.P.Q.2d 1001, 1005-07 (Fed. Cir. 2006) (***affirming the Board***, and holding that the description of a "poxvirus" was adequate, even though specification

did not describe ***any*** species related to the genus of poxviruses, where accessible literature sources clearly provided, as of relevant date, nucleotide sequences of poxvirus genes and their "essential regions"); *cf. Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997) (holding that the "possession" test does not require actual physical possession of the claimed product).

B. The rejection.

The Office cites MPEP § 2163 for the proposition that factors relevant to a determination of written description include the "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention."

The Office relies on the rationale applied in *Regents Univ. Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997), but *Eli Lilly* is inapt in this context, as *Eli Lilly* and its progeny pertain, at best, only to the description requirement relating to the disclosure of a single species of a genus of compounds of ***unknown*** structure. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1361, 65 U.S.P.Q.2d 1385, 1421 (Fed. Cir. 2003) (Clevenger, J., dissenting) (regarding the description provided for "exogenous gene," noting that "the majority, dismissing *Eli Lilly* on the grounds that no undisclosed DNA molecule appears in this case, verges on confining *Eli Lilly* to its facts").

Notably, the Board in *Capon* relied on *Eli Lilly* to assert that the specifications at issue did not provide the requisite description of the full scope of the recited genus of chimeric genes because the genes were not described by "structure, formula, chemical name, or physical properties," but only "in terms of the functional characteristics of the protein[s] [they] encode." *Capon*, 418 F.3d at 1354-55, 76 U.S.P.Q.2d at 1082. The Board specifically noted that neither specification provided a single example within the claimed genus. *Capon*, 418 F.3d at 1356, 76 U.S.P.Q.2d at 1083. The Federal Circuit ***reversed***, holding that the recited genus was adequately described with reference to the state of the art, which provided knowledge of the structure and function of the recited molecules. *Capon*, 418 F.3d at 1357, 76 U.S.P.Q.2d at 1085.

The Examiner specifically cites *In re Wilder*, 736 F.2d 1516, 1521, 222 U.S.P.Q. 369, 372-73 (Fed. Cir. 1984) in its rationale for the written description rejection. *Wilder* is of little relevance in the present context, because *Wilder* pertains to the issue of whether the title of the application and a broadly worded description of a figure can provide written support in a reissue proceeding, which issue is not present here.

The Examiner alleges that the generic expressions "bait fusion proteins", "fluorogenic fragment of fluorescent protein", "first peptide of interest," "linker protein", "prey fusion protein", "second peptide of interest" and "second linker" do not provide ample written description for the "compounds" since the claims do not describe a single structural feature. The Examiner alleges that the specification does not clearly define or provide examples of what qualifies as compounds of the invention.

It must be noted that it is the specification, not the claims themselves, that must provide adequate description of the invention *that is claimed.* Thus, it is not necessary that the claim terms themselves satisfy the written description requirement. That is the function of the specification, which is considered in view of the state of the art and the level of skill in the art.

(i) "fluorogenic fragment of fluorescent protein"

Fluorescent proteins are a well-characterized genus of molecules. As noted by the Examiner, the specification identifies examples of fluorescent proteins, such as RFP, BFP, YFP and CFP, and variants of GFP. Thus, the specification, in view of the knowledge of the art, provides an adequate written description of the genus of fluorescent proteins.

The expression "fluorogenic fragment of fluorescent protein" is likewise supported by the written description of the specification, given the knowledge of the art. The expression encompasses a fragment of a fluorescent protein embracing the structural feature that the fragment may functionally associate with a complimentary fragment to generate a fluorescent signal. A person skilled in the art would be aware that fluorescent proteins may be cleaved to form two fragments, which may functionally associate with each other when brought together in the appropriate orientation and form a species capable of generating a fluorescent signal. A person skilled in the art would also appreciate that the split point where the fluorescent protein is to be cleaved to originate the two fluorogenic fragments is to be chosen judiciously, so that the

two fluorogenic fragments are able to functionally associate with each other when brought together in the appropriate orientation and generate a fluorescent signal after such functional association. This knowledge is appropriately supported in the specification. A representative sub-genus of "fluorogenic fragment of fluorescent protein" is described at length at page 11 of the specification with regard to the Enhanced Green Fluorescent Protein (EGFP), a well-known fluorescent protein. Approximately 14 potential split points in EGFP are described giving rise to fluorogenic fragments. In view of this teaching provided for EGFP, a representative fluorescent protein, and armed with the knowledge provided in the art, the skilled person would know how to generate and test suitable split points in other fluorescent proteins to obtain fluorogenic fragments. Thus, it is believed that these representative species adequately describe the genus across its breadth.

(ii) "first peptide of interest" and "second peptide of interest"

In relation to the terms "a first peptide of interest" and "a second peptide of interest", it is submitted that the nature of the invention would not allow a restriction of these terms by a further structural definition. It is clear from the teaching on page 13 of the specification that a peptide of interest may be a small peptide or a full size protein, and these may be provided in different ways. Furthermore, as supported throughout the specification, such as on page 6, lines 5-7, in one embodiment of the invention there is provided a screening method that may be used to determine whether and/or how the first peptide of interest and the second peptide of interest interact. In this embodiment, the invention does not require prior knowledge of the possible interaction of the peptides of interest, let alone knowledge of the amino acid sequence or structure of the peptides of interest. Restriction of the nature of such peptides of interest to a limiting structural definition would thus unduly negate the nature of the invention.

It is submitted that the terms "a first peptide of interest" and "a second peptide of interest" have adequate written description in the specification and are sufficient to reasonably convey to a person skilled in the art that the inventor, at the time the application was filed, had possession of the entire scope of the claimed invention.

(iii) "linker portion" and "second linker portion"

Without acquiescing in the rejection, and in an effort to advance prosecution, claim 1 has been amended to more clearly define the structure of the "linker portion" and "second linker portion". Amended claim 1 specifies that the linker portion and the second linker portion independently comprise multiples of a pentapeptide sequence glycyl-glycyl-glycyl-glycyl-serine (GGGGS). The amendment is supported in the specification at page 9, lines 17-20. The amendment overcomes the ground of rejection as to the alleged lack of adequate written description for the terms "a linker portion" and "a second linker portion".

(iv) "bait fusion protein" and "prey fusion protein"

A "bait fusion protein" is recited in claim1 as comprising a first fluorogenic fragment of fluorescent protein, a first peptide of interest, and a linker portion interposed between the first peptide and the first fluorogenic fragment. A "prey fusion protein" is recited in claim 1 as comprising a second fluorogenic fragment of fluorescent protein, which is complementary to the first fluorogenic fragment of fluorescent protein, a second peptide of interest, and a linker portion interposed between the second peptide and the second fluorogenic fragment.

As discussed above, Applicants submit that the specification provides adequate written description for each of the components. Accordingly, it is submitted that the specification also provides adequate written description for the terms "a bait fusion protein" and "a prey fusion protein".

As acknowledged by the Examiner, at page 10 of the office action, the application discloses in Example 2 details of a protein interaction system as claimed, having suitable fluorogenic fragments of GFP, linkers of varying lengths, and exemplary leucine zipper proteins known to interact, wherein such leucine zipper proteins correspond to the first peptide of interest and second peptide of interest. This exemplary model of the protein interaction system provides a proof of the principle of the claimed system, since the ability of the fluorogenic fragments to interact and generate fluorescence was, in one aspect, associated with the fact that the leucine zipper proteins bind to each other. The amino acid sequences of the leucine zipper proteins or knowledge of their structures are immaterial for the implementation of the invention. This example thus demonstrates that other bait and prey protein combinations may be used. While the

Examiner notes that this means the numbers of possible prey and bait proteins are vast, as these prey and bait proteins will be attached to the respective linkers in the same way, the actual amino acid sequences of the bait and prey proteins are immaterial to putting the invention into effect.

The Examiner has asserted that the specification does not describe the kind or size of different proteins from the myriad of known proteins that can be fused to GFP without destroying the function of GFP. However, in one embodiment of the invention, linkers of suitable length and character are provided, as defined in the amended claim, such that, in contrast to the prior art, any proteins may be selected as bait and prey peptides of interest as they will not prevent the binding of fluorogenic fragments.

As pointed out in the previous section, the amendment of claim 1 with respect to the structural characteristics of the linker and second linker is believed to overcome the Examiner's objection.

It is therefore submitted that the specification successfully conveys to a person skilled in the art that the inventors had possession of the entire scope of the claimed invention at the time the application was filed. Applicants further submit that the nature of the invention does not allow for further structural definitions of the technical features of claim 1 without unduly restricting the scope of the claims.

In summary, Applicants submit that the claims as amended are supported by an adequate written description. Reconsideration and withdrawal of the rejection of claims 1, 3 and 5-13 under 35 U.S.C. § 112, first paragraph, for alleged lack of written description is respectfully requested.

Response to 35 USC 112 1st Paragraph Rejection – Enablement

There is a strong presumption that the specification, which discloses how to make and use the invention, complies with the enablement requirement of the first paragraph of 35 U.S.C. 112, unless there is reason to doubt the objective truth of the specification. *In re Marzocchi*, 169 USPQ 367, 370 (CCPA 1971). MPEP 2163.04. In establishing a prima facie basis to deny patentability under the first paragraph of 35 U.S.C. 112 for lack of adequate enabling support, it is incumbent upon the examiner to explain why he doubts the truth or accuracy of the supporting

specification and to buttress assertions with evidence or cogent reasoning inconsistent with the specification. *In re Strahilevitz*, 212 USPQ 561 (CCPA 1975); *In re Bowen*, 181 USPQ 48 (CCPA 1947); *In re Marzocchi*, supra. "Any assertion that the enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubts so expressed." *In re Dinh-Nguyen*, 181 USPQ 46, 47 (CCPA 1974).

What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail to satisfy the enablement requirement. "A patent need not disclose what is well-known in the art." *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). "A patent need not teach, and preferably omits, what is well-known in the art." *Spectra-Physics, Inc. v. Coherent, Inc.*, 3 U.S.P.Q.2d 1737, 1743 (Fed. Cir. 1987), cert. denied, 108 S.Ct. 346 (1987); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, supra. The specification may assume "that which is common and well-known" to persons skilled in the relevant art. *Webster Loom v. Higgins*, 105 U.S. 580 (1981). Also see M.P.E.P. 601.

Applicants respectfully submit that the description of the present application discloses the invention in a manner sufficiently clear and complete for it to be performed by a person skilled in the art without undue experimentation.

The fluorogenic fragments of claim 1 have been enabled by the description of features of the technical procedure to be followed to provide such fragments. As is clear from both the art and the description of the fluorogenic fragments of fluorescent protein provided in the present application, a number of different split points may be chosen to generate fragments of fluorescent proteins, such that, when these fragments functionally associate with each other, they generate a fluorescent signal capable of being detected. Applicants thus submit that a person skilled in the art may easily overcome any alleged unpredictability issues raised by the Examiner with respect to amino acid substitution in the fluorogenic fragments (regarding effects on folding, protein structure, function and fluorescence) by determining if fragments produced from a fluorescent protein could functionally associate with each other to generate a fluorescent signal capable of being detected. Applicants submit that this determination would not require painstaking experimental study or undue experimentation by those skilled in the art.

In another aspect, the description provides instructions as to possible split points of EGFP such that it would be clear to a person skilled in the art how to provide such fluorogenic fragments in other fluorescent proteins, such as, for example, other variants of green fluorescent protein. Furthermore, without undue experimentation, a person skilled in the art could readily determine if fragments produced from any chosen fluorescent protein could functionally associate with each other to generate a fluorescent signal capable of being detected, given the teaching in the present application and the art, for example, the document of Hamilton et al. Applicants agree with the Examiner that the relative skill of those in the art is high and believe that the amount of direction or guidance presented is sufficient that a person skilled in the art could apply the teaching presented in relation to EGFP to variants of GFP, such as yellow, blue or cyan fluorescent protein, and could without undue experimentation readily determine if fragments produced from these fluorescent proteins could functionally associate with each other to generate a fluorescent signal capable of being detected. Furthermore, a person skilled in the art could determine without undue experimentation whether a peptide of interest could be fused to a fluorogenic fragment. Therefore, Applicants submit that the fluorogenic fragments pertaining to EGFP and other fluorescent proteins have been properly enabled.

Applicants note that the linker and second linker portion of claim 1 have been amended to independently comprise multiples of the pentapeptide sequence GGGGS. Without acquiescing in the enablement rejection by the Examiner in the Office Action, Applicants submit that this amendment makes moot the Examiner's remarks on page 19, first complete paragraph, and on page 21, first complete paragraph, of the Office Action concerning the alleged unduly burden associated with amino acid substitution on the linker. Therefore, Applicants submit that the linker and the second linker have been properly enabled.

Applicants further note that, as stated in claim 1, the interaction of the first peptide of interest and the second peptide of interest within the protein interaction system allows for the fluorogenic fragments of the fluorescent protein to functionally associate and promote fluorescence. Applicants respectfully submit that the level of experimentation required to make the protein interaction system of claim 1 would not constitute undue experimentation, given that a person skilled in the art could readily determine whether a first peptide of interest linked to a

fluorogenic fragment through a linker portion could interact with a second peptide of interest linked to a complimentary fluorogenic fragment through a second linker portion, by determining whether the fluorogenic fragments could functionally associate to generate a fluorescent signal.

Based on the arguments presented above, Applicants submit that the claims as amended are enabled. Reconsideration and withdrawal of the rejection of claims 1, 3 and 5-13 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement is respectfully requested.

Response to 35 USC 102 Rejections

Hu *et al.*

Claims 1, 8-11 and 13 have been rejected as being allegedly anticipated by Hu *et al.*

Hu *et al.* does not disclose a protein interaction system comprising a plurality of bait fusion proteins comprising linker portions interposed between a first peptide and a first fluorogenic fragment wherein the linker portions of each bait fusion protein are of different lengths comprising multiples of a pentapeptide sequence glycyl-glycyl-glycyl-glycyl-serine. Claim 1 as amended is not anticipated by Hu *et al.*

Claim 1 further distinguishes over Hu *et al.* in other respects. Hu *et al.* provides plasmid expression factors for both an *E. coli* system and a mammalian expression system wherein different YFP fragments are attached to the bZIP domains of either Jun or Fos. In relation to claim 1, either Jun or Fos could be considered a first peptide of interest in a bait fusion protein and the other could be considered a second peptide of interest in a prey fusion protein.

While a range of different fluorescent fragments are disclosed by Hu *et al.*, in all cases described for the *E. coli* expression factors the linker sequence RSIAT is interposed between Jun and the N terminus of the respective fluorescent fragment, and the linker sequence KQKVNNH is interposed between Fos and the C terminus of the respective fluorescent fragment. At no point does Hu *et al.* teach different linker lengths being used in relation to Jun (a first peptide) and a fluorogenic fragment; nor does Hu *et al.* teach different linker lengths being used in relation to Fos (a second peptide) and a fluorogenic fragment.

Claim 1 requires a plurality of bait fusion proteins comprising a first fluorogenic fragment, a first peptide of interest and a linker portion interposed between the first peptide and

the first fluorogenic fragment. It further requires that the linker portions of each bait fusion protein are of different lengths and that the first peptide of interest is identical in each bait fusion protein. As Hu *et al.* discloses only a single linker length (that is, RSIAT for Jun and KQKVNNH for Fos) between a first peptide of interest and a first fluorogenic fragment, Hu et al. does not anticipate claim 1.

Accordingly, claim 1 is not anticipated by Hu *et al.* Claims 8-11 and 13 depend from claim 1, and recite additional features of the claimed protein interaction system. Claims 8-11 and 13 therefore do not lack novelty over Hu *et al.*

Hamilton *et al.*

Claims 1 and 5-13 are rejected as being allegedly anticipated by Hamilton *et al.*

Hamilton *et al.* does not disclose a protein interaction system comprising a plurality of bait fusion proteins wherein each bait fusion protein comprises a linker portion interposed between a first peptide and a first fluorogenic fragment wherein the linker portions of each bait fusion protein are of different lengths comprising multiples of a pentapeptide sequence glycyl-glycyl-glycyl-glycyl-serine. Claim 1 as currently amended is therefore novel over Hamilton *et al.* Claims 5 to 13 are dependent on claim 1 and are therefore also novel over Hamilton *et al.*

Response to 35 USC 103 Rejection

Claims 1 and 3-13 have been rejected as allegedly unpatentable over Hu *et al.* in view of hamilton *et al.*, as evidenced by http://www/biovioisno.com/updated/egfp.htm ("BioVision")/

As noted above, neither Hu *et al.* nor Hamilton *et al.* disclose linker portions interposed between the first peptide and first fluorogenic fragment wherein the linker portions of each bait fusion protein are of different lengths comprising multiples of a pentapeptide sequence glycyl-glycyl-glycyl-glycyl-serine. Such sequences have been shown by the inventors of the present application to provide advantageous flexibility properties which enable the linker region to be readily extended (page 15, lines 7 to 10 of the present application). Neither *Hu et al.* nor Hamilton *et al.* provide any indication that such linker portions would be advantageous or would maximize the chances of an interaction between peptides of interest being detected. The

deficiency is not remedy by BioVision. Hence, the combination of references does not result in the claimed invention. The claimed invention therefore would not have been obvious to one of ordinary skill in the art at the time the invention was made.

The invention of claim 1 is clearly patentable over Hu *et al.* and Hamilton *et al.*, as evidence by BioVision, for yet other reasons. The Examiner alleges that it would have been obvious to a person of ordinary skill in the art to try different linker lengths for optimal lengths for the fluorescent fragments to associate with each other to generate a fluorescent signal. The Applicants submit that this is not the case, as there is no teaching in the prior art documents that the provision of a protein interaction system comprising different linker lengths between a first peptide and a first fluorogenic fragment in a plurality of bait fusion proteins (wherein the first peptide of interest of each bait fusion protein is identical to the first peptide of interest in each of the other bait fusion proteins) would be advantageous. Specifically there is no suggestion that this would increase the chance of correct association between a bait fusion protein and a prey fusion protein. Moreover, Hamilton *et al.* specifically teaches at paragraph 12 that a linker length having 4-6 amino acids is sufficient and long unstructured linkers would be prone to proteolytic cleavage and be less stable. Prior art must be considered in its entirety, including disclosures that teach away from the invention of the claims under examination. The totality of a reference's teaching must be considered. A prior art reference that "teaches away" from the claimed invention is a significant factor to ne considered in determining obviousness. MPEP 2145(X.)(D.) Also *see*, *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 220 USPQ 303, 311 (Fed.Cir.1983), *cert. denied*, 469 US 851 (1984).

Accordingly, the skilled person upon reading the prior art would have no motivation to consider providing a protein interaction system comprising linker portions as claimed in claim 1, wherein the linker portions of each bait fusion protein are of different lengths comprising the specified pentapeptide sequence. Indeed, the skilled artisan would be led away form such an arrangement by the teachings of Hamilton *et al.*

Accordingly, Applicants submit that claim 1 as amended is allowable over the combination of Hu *et al.* and Hamilton *et al.*, as evidence by BioVision. Claims 3 to 13 are

dependent on claim 1 and therefore also therefore allowable over the asserted combination of references.

Conclusion

The claims remaining in the application are believed to be in condition for allowance. An early action toward that end is earnestly solicited.

Respectfully submitted,

JOHN NELSON, et al.

BY _____

DANIEL A. MONACO
Registration No. 30,480
DRINKER BIDDLE & REATH LLP
One Logan Square
18th and Cherry Streets
Philadelphia, PA 19103-6996
Tel.: (215) 988-3304
Fax: 215) 988-2757
Attorney for Applicants

APPENDIX A

Protein interaction system